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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/466,698	06/06/95	SANSONETTI P	2356.0043-02

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EXAMINER	
CAPUTA, A	
ART UNIT	**PAPER NUMBER**
1817	

DATE MAILED: 09/26/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.	Applicant(s)
08/466,698	Sansonetti et al.
Examiner	**Group Art Unit**
Anthony C. Caputa	1817

THE PERIOD FOR RESPONSE: [check only a) or b)]

a) ☒ expires 4 months from the mailing date of the final rejection.

b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☒ Appellant's Brief is due two months from the date of the Notice of Appeal filed on Aug 29, 1997 (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on _____ has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

☒ The proposed amendment(s):

☒ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

☐ will not be entered because:

☐ they raise new issues that would require further consideration and/or search. (See note below).

☐ they raise the issue of new matter. (See note below).

☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

☒ Applicant's response has overcome the following rejection(s):
The prior rejection of claims 13 and 14 under 35 USC 112, second paragraph

☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☒ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:
see attachment

☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: _____

Claims objected to: _____

Claims rejected: *1-10, 13, and 14*

☐ The proposed drawing correction filed on _____ ☐has ☐has not been approved by the Examiner.

☒ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). 14 .

☒ Other *see Interview Summary-Paper No. 15*

ANTHONY C. CAPUTA
PRIMARY EXAMINER
GROUP 1800

1. Claims 1-10, 13, and 14 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the last Office Action.

As set previously, it is apparent that numerous modified Shigella are required to practice the claimed invention.

In the instant case the construction of claimed Shigella mutants requires knowledge of the nucleotide sequence of said genes, which regions are responsible for biological activity, and the number of nucleotides which must be deleted or inserted. Due to the limited teaching of the specification and the unpredictable nature of which mutations are useful one skilled in the art can not practice the invention as claimed absent undue experimentation. In view of the foregoing the only means by which applicants can provide an enabling disclosure for the Shigella mutants is by depositing said mutants and limiting the claims to the deposited mutants.

Applicants urge that the specification provides sufficient teachings for one skilled in the art to practice the claimed invention. Applicants state that the specification teach of methods of modification to employ in order to inactivate the genes. These arguments are not considered persuasive. The decisional law has held the mere recitation in the specification of a broad concept does not necessarily provide a sufficient basis for broadly claiming it (i.e. transposon mutagenesis). See Ex parte Gardner 157 USPQ 162 (Bd. Pat. Appls and Interf. 1967), In re Cavallilo, 127 USPQ 202 (CCPA 1969). The fact that the terms in a claim are the same as those in the specification does not prevent the claims from being rejected as unduly broad if they define subject matter not define subject matter not described to be the actual invention by means of adequate representative samples. See in re Lund, 153 USPQ 625 (CCPA 1967). In the instant case the construction of claimed Shigella mutants requires knowledge of the nucleotide sequence of said genes (iscA, virG, aerobactin, enterochelin), which regions are responsible for biological activity, and the number of nucleotides which must be deleted or inserted. Due to the limited teaching of the specification and the unpredictable nature of which mutations are useful one skilled in the art can not practice the invention as claimed absent undue experimentation. In view

of the foregoing the only means by which applicants can provide an enabling disclosure for the Shigella mutants is by depositing said mutants and limiting the claims to the deposited mutants.

While it would appear techniques are known in the art for inactivation, as pointed out by applicants it is **not** routine in the art to screen for positions within the DNA sequence of the gene so that it does not invade the cells, spread within infected cells, or not produce toxins. Because the specification does **not** disclose :

- which regions of the genes are responsible for biological activity;
- the number of nucleotides which must be deleted or inserted;
- the identity of the genes that are responsible for invading cells, not producing toxins, etc.;
-more than one genes would be expected to be involved in toxin production, spreading, and/or invasion;
- no guidance as to which of the essentially infinite possible choices is likely to be successful;

modifications that can be made to inactivate the genes is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Beyond the reasons set forth above, while it may be true that the prior art teaches of iscA; virG; aerobacterin; eneterocholin, and the Shiga toxin gene as set forth by applicants said evidence is not commensurate in scope with the claimed invention which encompasses the inactivation of gene responsible for invasion, spreading, and toxin production.

Applicants argue that a deposit is not required since the specification is clearly enabled. Applicants argument is not persuasive. It is the Examiner position that the specification is not enabled for the reason set forth above.

Applicants newly argue that Nassif et al., Baudry et al., and Maurelli et al contain the teachings necessary for screening the *Shigella* genes involved in the invasion of cells, spreading

within infected cells, etc.. Applicants arguments are not persuasive. Nassif et al. (Infection and Immunity 55(9):1963-69 1987) reference is only directed to iuc::TN10 mutant. Applicants specific arguments directed to Baudry et al and Maurelli et al can not considered since these references were not provided or cited in applicants' response submitted August 29, 1987. Beyond the reason set forth above, applicants arguments are not sufficient to obviate the rejection in view of *Fliers v. Sugano,* 25 USPQ 2d 1601 (Fed. Cir. 1993) were it is stated: "if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is until after gene has been isolated; thus regardless of complexity or simplicity of method of isolation employed, conception of any chemical substance, requires definition of the substance other than by its functional utility. Additionally, the Federal Circuit in *Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., and Genetics Institute., Inc.,* 18 USPQ 2d 1016 (Fed. Cir. 1991) refused to find that despite the high degree of homology between the human and monkey DNA, the human EPO gene would have been isolatable using the monkey EPO gene.

For the reasons set forth above and in the last Office Action said rejection is maintained.

2. The prior provisional rejection of claim 13 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending application Serial No. 08/118,100 is maintained for the reasons set forth in the previous Office Actions.

Applicants request to hold this rejection in abeyance until allowable subject matter has been indicated in either case. The Examiner notes that USSN 08/118,100 has been allowed. Until applicants submit a proper terminal disclaimer said rejection is maintained.

3. The prior rejection of claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph is withdrawn in view of applicants amendment.

4. Any inquiry concerning this communication should be directed to Dr. Anthony C. Caputa, whose telephone number is 703-308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is 703-308-0196.

Papers related to this application may be submitted to Group 1817 by facsimile transmission. Papers should be faxed to Group 1817 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703)-308-4242.

Anthony C. Caputa, Ph.D.

September 26, 1997

ANTHONY C. CAPUTA
PRIMARY EXAMINER
GROUP 1800